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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/431,843 11/02/99 ZAGON I 98-1984-

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EXAMINER

LANDSMAN, R

ART UNIT

PAPER NUMBER

1647

14

DATE MAILED:

01/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/431,843

Applicant(s)

ZAGON ET AL.

Examiner

Robert Landsman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 October 2000.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 and 14-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 14-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8.
- 18) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☒ Other: Sequence Comparisons A-J.

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DETAILED ACTION

1. Formal Matters

- A. Amendment B, filed 10/16/00, has been entered into the record.
- B. Claims 1-37 are pending in the application and were subject to restriction. Applicants have elected claims 1-8 and 14-17, with traverse. The Examiner further required the of one of the seven nucleic acid sequences (SEQ ID NO:1, 4, 5, 7, 9, 11 and 13). However, during a telephone interview on with Frank DiGiglio on 9/6/00, it was brought to the attention of the Examiner that SEQ ID NO:4, 5, 7, 9, 11 and 13 were all splice variants of a human OGF receptor whereas SEQ ID NO:1 was a rat OGF receptor. Applicants have argued that if the Examiner maintains the current restriction with regard to SEQ ID NO:1, 4, 5, 7, 9, 11 and 13, that they are concerned that claims pursued in a divisional application may be alleged as "obviousness-type" double patenting. However, the Examiner holds that since SEQ ID NO:1 is independent and distinct from SEQ ID NO:4, 5, 7, 9, 11 and 13. Therefore, SEQ ID NO:1 would not be obvious over SEQ ID NO:4, 5, 7, 9, 11 and 13. However, the Examiner has determined that there would not be an undue search burden to search SEQ ID NO:1 along with SEQ ID NO:4, 5, 7, 9, 11 and 13. Therefore, the election of species is withdrawn and all of the elected claims (1-8 and 14-17) will be examined in their entirety in the present application.

2. Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

- A. Claims 1-8 and 14-17 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility. These claims are drawn to an invention with no apparent or disclosed patentable utility. This rejection is not in conflict

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with the current utility guidelines. The instant application has provided a description of nucleic acid molecules which encode a partially isolated protein. However, the instant application does not disclose the biological role of this protein or its significance.

It is clear from the instant specification that the claimed nucleic acids encode an "orphan receptor" in the art. There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Applicants' claimed invention is incomplete.

The instant situation is directly analogous to that of which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed "real-world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility," "[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form - there is insufficient justification for permitting an applicant to engross what may prove to be a broad field," and "a patent is not a hunting license," "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a protein which has a yet undetermined function or biological significance. Applicants have disclosed that they are in possession of compounds which *bind* various opioid receptors in tissue containing the receptors of the invention, however, Applicants have not demonstrated that these receptors themselves actually bind opioid ligand. Applicants conclude that the

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receptors of the invention are opioid receptors based only on tissue localization and homology. Applicants do demonstrate that human OGF α antisense does increase cell numbers in culture (page 47 of the specification). However, this has not been demonstrated to act via the claimed receptors. Therefore, there is no actual and specific significance which can be attributed to said proteins identified in the specification. For this reason, the instant invention is incomplete. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which bind to and/or mediate activity of the said receptor is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for said protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful. **In addition, since the nucleic acids do not possess a specific, substantial and credible asserted utility or a well established utility, then the vectors, host cells, antisense molecules, methods of producing the proteins and the pharmaceutical compositions also do not possess a specific, substantial and credible asserted utility or a well established utility.**

3. Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. The specification is objected to and claims 1-8 and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

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B. Claims 1-8 and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, Applicants have provided no guidance or working examples that the proteins encoded by SEQ ID NO:1, 4, 5, 7, 9, 11 or 13 are opioid growth factor receptors. Applicants have not provided, for example, any binding data using these isolated sequences, nor is it predictable to one of ordinary skill in the art that these receptors bind opioid ligands, or are, in fact, opioid growth factor receptors. Applicants only state that these receptors are homologous to other known receptors and that they have been isolated from cells which bind labeled opioid-specific compounds.

Furthermore, the breadth of claims 1 and 7 are extensive with regard to claiming all “OGFr proteins,” and “fragments” of the proteins encoded for by SEQ ID NO:1, 4, 5, 7, 9, 11 and 13. A fragment can be as little as one amino acid and Applicants provide no guidance or working examples of how to produce a functional fragment, or what the function of these fragments would be. Furthermore, it is unpredictable to one of ordinary skill in the art how to make and/or use a functional fragment of the invention.

Also, regarding claim 3, the breadth of the claim is extensive with regard to claiming all nucleic acid molecules which are “substantially homologous” to, or in which the “complement” hybridizes to SEQ ID NO:1, 4, 5, 7, 9, 11 and 13. The specification does not provide guidance or working examples of what the function of all nucleic acid molecules is, nor, regarding claim 4, does it provide any guidance or

working examples of what the “**antisense**” to these SEQ ID NOs would encode, or what their function would be. Furthermore, it is not *predictable* to one of ordinary skill in the art what the functions of these “substantially homologous,” “antisense” nucleic acids, molecules in which the “complement” hybridizes to SEQ ID NO:1, 4, 5, 7, 9, 11 and 13, the proteins, or protein fragments, which they encode, are. Nucleic acid molecules which hybridize to a sense strand, such as to SEQ ID NO:1, 4, 5, 7, 9, 11 and 13 would produce antisense DNA and it is not known, nor is it predictable to one of ordinary skill in the art, what the activity or function of these antisense molecules is.

Finally, regarding claims 14-17, Applicants have not provided any guidance or working examples of any “**pharmaceutical composition**” in the claims or in the specification for any of the molecules in this rejection. Applicants have not provided any diseases which can be treated using the nucleic acid molecules of the invention, nor have they provided a dosing regimen, or in any way enabled one of ordinary skill in the art to make and/or use the claimed pharmaceutical composition.

In summary, Applicants have provided no guidance or working examples that the SEQ ID NOs of the invention are, in fact, opioid growth factor receptors. Furthermore, the breadth of the claims is extensive with regard to Applicants claiming a method of producing all OGFr proteins, as well as claiming nucleic acids which encode fragments of, or are substantially homologous to, SEQ ID NO:1, 4, 5, 7, 9, 11 and 13 as well as claiming all nucleic acid molecules which in which the complement hybridizes to these SEQ ID NOs. There is also a lack of guidance and working examples of these fragments as well as for the molecules which in which the complement hybridizes to these SEQ ID NOs as well as for the antisense nucleic acid molecules which hybridize to the claimed SEQ ID NOs. Applicants do not provide a function of these nucleic acid molecules, or a function of the proteins which they encode. Finally, Applicants do not provide any guidance or working examples of pharmaceutical compositions comprising the claimed nucleic acid molecules. These factors, along with the lack of

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predictability to one of ordinary skill in the art as to what the functions of all of these molecules are, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

4. Claim Rejections - 35 USC § 112, first paragraph – lack of written description

A. Claims 1-8 and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. These claims refer to all “OGFr proteins”, “fragments” of proteins encoded for by SEQ ID NO:1, 4, 5, 7, 9, 11 and 13, nucleic acid molecules which are “**substantially homologous**” to said SEQ ID NOs, “**antisense**” to said SEQ ID NOs as well as nucleic acid molecules in which the “**complement**” hybridizes to said SEQ ID NOs.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:1, 4, 5, 7, 9, 11 and 13, substantially homologous nucleic acids and molecules in which the complement hybridizes to said SEQ ID NOs, (which could be at least thousands of molecules) alone are insufficient to describe the genus.

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One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

5. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 and 14-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1-5 and 8 are confusing since they recite "any of SEQ ID NO..." It is not clear whether the isolated nucleic acid molecule of the invention can comprise, for example, a fusion of SEQ ID NO:1 and 3 together, or if the claim is drawn toward "any *one* of SEQ ID NO..." It is suggested that the claims be amended to recite "...any one of SEQ ID NO:..." Claims 6 and 14-17 are rejected since they depend from rejected base claims.

B. Claim 3, 5, 6, 16 and 17 are confusing. Claim 3 recites "stringent conditions." However, it is not clear what the metes and bounds of "stringent conditions" are. Nucleic acid molecules which hybridize under low stringency may not hybridize under "moderately stringent conditions" or "highly stringent conditions." Applicants provide on page 13, lines 31 to page 14, line 9 of the specification an example of "stringent conditions." However, the exact hybridization conditions, including the wash step, must be recited in the claim. Claims 5, 6, 16 and 17 are rejected since they depend from rejected base claims.

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C. Claim 7 is rendered vague and indefinite because of the term "OGFr." This is an acronym and does not distinctly point out the claimed invention. The name of the protein is arbitrary and proteins can have more than one name, or the name of a protein can change. It is, therefore, required that the claim be amended to recite the SEQ ID NOs of the claimed invention. This rejection can be overcome by including the limitations of claim 8 (i.e. the SEQ ID NOs) in claim 7. Claim 8 is objected to since it depends from rejected claim 7.

6. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 1-3, 5, 14 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonaldo et al. The claims teach an isolated nucleic acid molecule comprising a fragment which is substantially homologous to SEQ ID NO:1 and which would hybridize under stringent conditions to SEQ ID NO:1. The claims also teach vectors and pharmaceutical compositions comprising these molecules. Bonaldo et al. teach an isolated nucleic acid molecule comprising a fragment of SEQ ID NO:1 and which is substantially homologous to SEQ ID NO:1. The nucleic acid of Bonaldo et al. would hybridize under stringent conditions to SEQ ID NO:1 (Sequence Comparison A). Bonaldo et al. also teach these nucleic acid molecules in a vector (Figures 3 and 4). One of ordinary skill in the art would immediately envision these plasmids in a pharmaceutical carrier, such as water or the buffer involved in the digestion of the plasmids in Figures 3 and 4.

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B. Claims 1, 5-7, 14, 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Pellett et al. The claims teach an isolated nucleic acid molecule comprising a fragment of SEQ ID NO:4, 5, 9 and 11, an expression vector, host cell, a method of making a fragment of an OGFr protein and a pharmaceutical composition. Pellett et al. teach an isolated nucleic acid molecule comprising a fragment of SEQ ID NO:4, 5, 9 and 11 (Sequence Comparisons B-E). Pellett et al. also teach an expression vector, host cell and a method of producing a fragment of an OGFr protein (page 522, right column under "Expression of 101K fragments..."). One of ordinary skill in the art would immediately envision these vectors in a pharmaceutical carrier, such as water or the buffer involved in the transformed E. coli cells and protein analysis (page 523 under "Protein analysis and immunoblot").

C. Claims 1, 5, 14 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Fliegel et al. The claims teach an isolated nucleic acid molecule comprising a fragment of SEQ ID NO:7, an expression vector and pharmaceutical compositions. Fliegel et al. teach an isolated nucleic acid molecule comprising a fragment of SEQ ID NO:7, and an expression vector (Sequence Comparison F; page 21523, "Experimental Procedures"). One of ordinary skill in the art would immediately envision these vectors in a pharmaceutical carrier, such as water or the buffer as described in the "Experimental Procedures" section.

D. Claims 1, 5, 14 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Everett et al. The claims teach an isolated nucleic acid molecule comprising a fragment of SEQ ID NO:13, an expression vector and pharmaceutical compositions. Everett et al. teach an isolated nucleic acid molecule comprising a fragment of SEQ ID NO:13 (Sequence Comparisons G). Everett et al. also teach an expression vector (page 1387, right column, first full paragraph). One of ordinary skill in the art would immediately envision these vectors in a pharmaceutical carrier, such as water or the buffer used to clone

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the nucleic acid molecules into expression vectors (page 1387, right column, first full paragraph; Figures 1 and 2).

E. Claims 1, 5-7 and 14-17 are rejected under 35 USC 102(e) as being unpatentable by Chambon et al. (US Patent No. 5,861,381). Chambon et al. teach a fragment of SEQ ID NO:5, 9, 11 and OGF α protein as well as a vector, host cell and method of making proteins encoded by these fragments (Sequence Comparisons H-J; column 8, lines 22-50). Chambon et al. also teach pharmaceutical compositions comprising these fragments (Abstract; Examples 1 and 3).

7. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

A. Claims 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over the three primary references Bonaldo et al., Fliegel et al., or Everett et al. each in view of Chambon et al. (US Patent No. 5,861,381). The claims teach a host cell and a method of producing proteins from transfected cells. Bonaldo et al., Fliegel et al. and Everett et al. teach an isolated nucleic acid molecule comprising a fragment of SEQ ID NO:1, 7 or 13, respectively and an expression vector as discussed in the above rejections under 35 USC 102(b). However, neither Bonaldo et al., Fliegel et al., or Everett et al. teach a cell transformed with an expression vector, or a method of producing a fragment of an OGF α protein. However, Chambon et al. do teach a cell transformed with an expression vector, or a method of producing a fragment of an OGF α protein (column 8, lines 22-50).

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Chambon et al. by substituting a cDNA in the polycloning region of the vector with the polynucleotide (cDNA) of either Bonaldo et al., Fliegel et al. or Everett et al. for the purpose of transfecting a host cell and, therefore, producing a protein of interest. One of ordinary skill in the art would have been motivated to make this substitution in order to express the protein encoded by the introduced DNA in a host cell to perform ligand binding and functional assays. There would have been a reasonable expectation of success for a person of ordinary skill in the art to make this invention since these techniques are widely used in the art and are highly successful. The present invention, therefore, is *prima facie* obvious over the above references in the absence of evidence to the contrary.

Advisory information

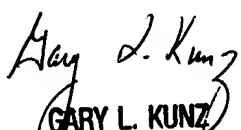
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
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January 02, 2001


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